PATENT COOPERATION TREATY

PCT

RECD 24 SEP 2001
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
15280-3912PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/19039	12/07/2000	13/07/1999
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant THE GOVERNMENT OF THE UNITED STATES OF AME..et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08/02/2001	20.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bladier, C Telephone No. +49 89 2399 7306

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/19039

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-59,59a,60,61 as originally filed

Claims, No.:

1-44 as originally filed

Drawings, sheets:

1/14-14/14 as originally filed

Sequence listing part of the description, pages:

1-10, filed with the letter of 22.10.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 20-42.

because:

   ☒ the said international application, or the said claims Nos. 20-42 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-44
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-44
Industrial applicability (IA)	Yes:	Claims	1-19, 43, 44
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. **Claims 20-42** relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Cited documents

2. Reference is made to the following documents:

   D1: DAVODEAU F. *et al.*, JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 268, no. 21, July 1993, p15455-15460
   D2: YOHIKAI Y. *et al.*, EMBL DABASE ENTRY HSTCRGAA4, ACCESSION NUMBER M27334, 2 February 1990
   D3: LEROY H., EMEST DATABASE ENTRY AI557112, ACCESSION NUMBER AI557112, 25 March 1999
   D4: VASMATZIS G., PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 95, January 1998, p300-304

Novelty - Article 33(2) PCT

3. The term 'TARP' used in the claims is an arbitrary designation meaningless for the person skilled in the art (see objection item VIII point 8). Thus, in absence of a reference to a specific amino acid sequence, said 'TARP' is interprated as 'any polypeptide'. Consequently,
   - the subject-matter of **claims 1-5** is anticipated by **any** polypeptide of the prior art,
   - the subject-matter of **claims 6-9** is anticipated by any composition of the prior art

comprising **any** polypeptide and a pharmaceutically acceptable carrier,
- the subject-matter of **claims 20-35** is anticipated by any method of the prior art comprising administering to a subject **any** polypeptide,
- the subject-matter of **claims 36-42** is anticipated by any method of the prior art comprising detecting **any** polypeptide,
- the subject-matter of **claim 43** is anticipated by any antibody of the prior art that binds to an epitope of **any** polypeptide,
- the subject-matter of **claim 44** is anticipated by any method of the prior art of modulating levels of **any** polypeptide in a cell.

Furthermore the use of unclear formulations such as 'fragment', 'epitope', 'with at least 90% sequence identity to TARP' (see Item VIII points 9-11), as well as the use of functional features rather than structural terms to define the subject-matter of the claims (see Item VIII point 12) broaden the scope of said claims and render it indistinguishable from the prior art.

4. The objection regarding 'TARP' designation also applies to the subject-matter of **claims 10-19.** Thus said subject-matter is anticipated by **any** recombinant nucleic acid of the prior art comprising a nucleotide sequence encoding **any** polypeptide.

Would a reference to SEQ ID N°13 be added, it is noted that:
- both documents D1 and D2 disclose a recombinant nucleic acid comprising a nucleotide sequence (D1, see accession number X72500; D2, see accession number M27334) which has 100% identity in 174 bp overlap with 74-247 fragment of SEQ ID N°13,
- document D3 also discloses a recombinant nucleic acid comprising a nucleotide sequence which has 99.4% identity over whole length with 74-247 fragment of SEQ ID N°13,
consequently those documents are prejudicial to the novelty of the subject-matter of **claims 10-19**.

Inventive step - Article 33(3) PCT

5. Would **claims 1-9 and 20-44** be rendered novel by inserting a reference to the amino acid sequence SEQ ID N°14 of TARP and by restricting their scope to the

specific polypeptide TARP of the invention, the IPEA is of the opinion that said claims would not involve an inventive step in the view of document D4. Indeed, said document reveals the existence of TCRγ mRNA in normal and cancer prostate cells (see page 304 note added in proof). Thus it would be obvious for the person skilled in the art to look for the product of traduction of said mRNA. Finding that a novel protein is translated *in vivo* from said mRNA, even if unexpected and involving a lot of work, would be achieved inevitably in the course of this work which is routine work for the skilled person. Consequently, the finding of TARP is regarded as an additional effect achieved by the skilled person on the basis of an obvious measure which could not substantiate inventive step.

Industrial applicability - Articles 33(1) and (4) PCT

6. For the assessment of the present **claims 20-42** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII
Certain defects in the international application

7. There are various inconsistencies in the description, particularly regarding references to Figures. For example,
- page 12 line 20, page 13 line 2, page 14 line 3, page 58 lines 13, 29, page 59 line 33, reference to figure 7A is incorrect since no figure 7A has been filed,
- page 13 lines 13 and 26, reference to figure 7C is incorrect since no figure 7C has been filed,
- page 13 line 30 and page 59 line 26, reference to figure 6A is incorrect since no figure 6A has been filed,
- page 15 line 4, a reference to Figure 3 A or B or C is missing,
- page 49 lines 14-15, it is written that four ATG are double underlined in Table 1, however this is not apparent from filed Table 1,

- page 51 lines 30-33 it is written that PS-TCRγ-1 is the 13 kDa protein and PS-TCRγ-2 is the 7.2kDa protein. This is in contradiction with the legende of Figure 1 which defines PS-TCRγ-1 as the 7.2kDa protein and PS-TCRγ-2 as the 13 kDa protein.
- page 58 line 6, reference to Figure 3 is incorrect .

These inconsistencies render the invention obscure and should be corrected according to Rule 5.1(iii) PCT.

Re Item VIII
Certain observations on the international application

8. The term 'TARP' is an arbitrary designation used by the applicant to characterize the polypeptide of the invention. Even if this designation is clearly defined in the description, it is not defined in the claims and therefore is meaningless for the skilled person (Article 6 PCT).

9. The term 'fragment' in **claims 1, 3, 10, 12, 17, 20 and 21** is vague and indefinite since it is unknown which deletions and/or variations are made and to which extent (structurally and functionally) said fragment differs from TARP. Consequently, this term is inadmissible under Article 6 PCT.

10. The term 'epitope' in **claims 20, 27, 29-33 and 43** is obscure since neither the composition nor the length of said epitope is given. Thus said epitope could be any part of TARP against which an antibody is produced. This encompasses a multitude of epitopes which will generate non TARP-specific antibodies (Article 6 PCT).

11. In **claims 1, 4, 5, 10, 13, 14, 18-20, 22 and 23**, the formulation 'a polypeptide with at least 90% sequence identity to TARP' is unclear since the length over which the polypeptide has at least 90% sequence identity to TARP is not specified. Said unclarity is prejudicial to the novelty of said claim since the length might be interpreted as 2-3 pb and hence a multitude of polypeptide of the prior art falls under the scope of said claims and anticipates them (Article 33(2) PCT). Furthermore it is noted that in general, variants of a sequence are allowed only if

those variants are limited to the function exhibited by the sequence from which they derived. In the present case, it is not specified that polypeptides with at least 90% sequence identity to TARP have the same function as TARP. That means that the subject-matter of claims 1, 4, 5, 10, 13, 14, 18-20, 22 and 23 is totally undefined functionally and thus inadmissible under Article 6 PCT.

12. The formulations 'which is specifically recognized by an antibody which specifically recognizes TARP' and 'when processed and presented in the context of MHC molecules activates T lymphocytes against cells which express TARP' in **claims 1, 4, 5, 10, 13, 14, 18, 19, 20, 22 and 23** are functional definitions that do not characterized the polypeptide in structural terms, but by means of its effect. This mode of definition does not relate to a tangible polypeptide but comprises an infinite number of possible alternatives, which may have quite different compositions. Consequently, the subject-matter for which protection is sought is not clearly defined contrary to Article 6 PCT.

13. The subject-matter of **claim 44** appears to be a mere desideratum which lacks support in the description (Article 6 PCT). In this respect, no ribozyme and no DNA-binding protein which specifically binds to a TARP-encoding nucleic acid has been exemplified in the description and there is no concrete example of any method that would fulfill the requirement set up in this claim.

14. The formulation of **claim 14** is unclear (Article 6 PCT) since it is not understandable:
- what is meant by the formulation 'and cells sensitized in vitro to TARP (line 19),
- to what refers 'an immunogenic fragment thereof' (line 20),
- why the subject-matter of lines 13-17 is repeated in lines 20-24.